

WHAT IS CLAIMED IS:

1. A method of detecting binding of a PAS domain with a foreign core ligand of the PAS domain, wherein the PAS domain is predetermined, prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, the  
5 method comprising the steps of:

detecting a first NMR spectrum of the PAS domain in the presence of a foreign  
ligand; and

comparing the first NMR spectrum with a second NMR spectrum of the PAS domain  
in the absence of the ligand to infer the presence the ligand specifically bound within the  
10 hydrophobic core of the PAS domain.

2. A method according to claim 1, the PAS domain is PAS kinase PAS A.